

CLAIMS

1. A composition comprising an isolated amino acid sequence that comprises a portion of SEQ ID NO:4, wherein said portion comprises SEQ ID NO:6 and has activity chosen from DNA nuclease activity and cell killing activity.

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2. The composition of Claim 1, wherein said portion comprises SEQ ID NO:7.

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3. A composition comprising a conjugate that comprises an amino acid sequence comprising SEQ ID NO:6, wherein said amino acid sequence is operably linked to a first molecule that specifically binds to a cell molecule.

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4. The composition of Claim 3, wherein said amino acid sequence comprises SEQ ID NO:7.

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5. The composition of Claim 3, wherein said amino acid sequence further comprises a N-terminal signal peptide.

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6. The composition of Claim 3, wherein said amino acid sequence further comprises a cell internalization peptide.

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7. The composition of Claim 3, wherein said amino acid sequence further comprises a nuclear localization peptide.

8. The composition of Claim 3, wherein said first molecule comprises an antibody.

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9. The composition of Claim 8, wherein said antibody specifically binds to cancer cells.

10. The composition of Claim 9, wherein said cancer cells are chosen from non-small cell lung carcinoma cells, breast cancer cells, gastrointestinal cancer cells, renal carcinoma cells, and liver cancer cells.

5 11. The composition of Claim 10, wherein said cancer cells comprise liver cancer cells.

10 12. The composition of Claim 11, wherein said liver cancer cells comprise hepatocellular cancer cells.

15 13. The composition of Claim 11, wherein said antibody that binds to liver cancer cells comprises an antibody chosen from Hepama-1, anti-PLC1, anti-PLC2, K-PLC1, K-PLC2, K-PLC3, 49-D6, 7-E10, 34-A4, 26-A10, 34-B9, 79-C8, 16-E10, 5D3, 5C3, 2C6, a-AFP, HP-1, hHP-1, mAb 95, YPC2/38.8, P215457, PM4E9917, HAb25, HAb27, KY-1, KY-2, KY-3, 9403 Mab, KM-2, S1, 9B2, IB1, A9-84, SF-25, AF-10, XF-8, AF-20, a-hIRS-1, FB-50, SF 31, SF 90, 2A3D2, and 2D11E2.

20 14. The composition of Claim 11, wherein said antibody that binds to liver cancer cells comprises Hepama-1 antibody.

25 15. The composition of Claim 14, wherein said antibody comprising Hepama-1 antibody is humanized.

16. The composition of Claim 9, wherein said cancer cells are chosen from B cell lymphoma cells, myeloid leukemia cells, renal carcinoma cells, colon cancer cells, pancreatic cancer cells, colorectal cancer cells, ovarian cancer cells, and prostate cancer cells.

30 17. The composition of Claim 3, wherein said first molecule comprises a ligand of a cell receptor.

18. The composition of Claim 17, wherein said ligand comprises a growth factor.

5 19. The composition of Claim 18, wherein said growth factor is chosen from epidermal growth factor, insulin-like growth factor, fibroblast growth factor, and vascular endothelial growth factor.

10 20. A composition comprising a nucleic acid sequence encoding an amino acid sequence that comprises a portion of SEQ ID NO:4, wherein said portion comprises SEQ ID NO:6, and wherein said amino acid sequence has activity chosen from DNA nuclease activity and cell killing activity.

15 21. The composition of Claim 20, wherein said portion comprises SEQ ID NO:7.

22. The composition of Claim 20, wherein said amino acid sequence further comprises one or more of N-terminal signal peptide, cell internalization peptide, nuclear localization peptide, and an antibody that specifically binds to biotin.

20 23. A composition comprising an expression vector that comprises a nucleic acid sequence encoding an amino acid sequence that comprises a portion of SEQ ID NO:4, wherein said portion comprises SEQ ID NO:6, and wherein said amino acid sequence has activity chosen from DNA nuclease activity and cell killing activity.

25 24. The composition of Claim 23, wherein said portion comprises SEQ ID NO:7.

30 25. A cell comprising an expression vector that comprises a nucleic acid sequence encoding an amino acid sequence that comprises a portion of SEQ ID NO:4, wherein said portion comprises SEQ ID NO:6, and wherein said amino acid sequence has activity chosen from DNA nuclease activity and cell killing activity.

26. The composition of Claim 25, wherein said portion comprises SEQ ID NO:7.

5 27. A composition comprising an antibody that specifically binds to SEQ ID NO:7.

10 28. The composition of Claim 27, wherein the binding affinity of said antibody to SEQ ID NO:7 is higher than the binding affinity of said antibody to SEQ ID NO:4.

15 29. The composition of Claim 27, wherein the binding affinity of said antibody to SEQ ID NO:6 is higher than the binding affinity of said antibody to SEQ ID NO:4.

20 30. The composition of Claim 27, wherein said binding reduces SEQ ID NO:7 activity chosen from DNA nuclease activity and cell killing activity.

25 31. A method for increasing cell death, comprising:

20 a) providing:

i) cells; and

ii) a composition comprising an amino acid sequence comprising SEQ ID NO:6; and

b) contacting said cells with said composition to produce contacted cells wherein said contacting increases cell death of said contacted cells.

25 32. The method of Claim 31, wherein said amino acid sequence comprises SEQ ID NO:7.

30 33. The method of Claim 31, wherein said amino acid sequence further comprises an antibody that specifically binds to said cells.

34. The method of Claim 31, wherein said method further comprises detecting increased cell death in said contacted cells.

5 35. The method of Claim 31, wherein said method further comprises, prior to step b), providing a nucleotide sequence encoding said amino acid sequence, and expressing said nucleotide sequence in said cells.

10 36. The method of Claim 31, wherein said cells are *in vitro*.

15 37. The method of Claim 31, wherein said cells are *in vivo* in a mammalian animal.

38. The method of Claim 37, wherein said mammalian animal is human.

39. The method of Claim 38, wherein said human is chosen from a human that has cancer and a human that is suspected of being capable of developing cancer.

40. The method of Claim 39, wherein said amino acid sequence further comprises an antibody that specifically binds to cancer cells in said cancer.

20 41. The method of Claim 39, wherein said cancer is chosen from liver cancer, gastric cancer, head cancer, neck cancer, lung cancer, breast cancer, prostate cancer, cervical cancer, pancreatic cancer, colon cancer, ovarian cancer, stomach cancer, esophagus cancer, mouth cancer, tongue cancer, gum cancer, skin cancer, muscle cancer, heart cancer, bronchial cancer, cartilage cancer, bone cancer, testis cancer, kidney cancer, 25 endometrium cancer, uterus cancer, bladder cancer, bone marrow cancer, lymphoma cancer, spleen cancer, thymus cancer, thyroid cancer, brain cancer, neuron cancer, gall bladder cancer, ocular cancer, joint cancer, glioblastoma, mesothelioma, lymphoma, leukemia, melanoma, squamous cell carcinoma, osteosarcoma, and Kaposi's sarcoma.

30 42. The method of Claim 41, wherein said cancer is liver cancer.

43. The method of Claim 42, wherein said antibody that specifically binds to liver cancer cells comprises Hepama-1 antibody.

5 44. A method for detecting cell apoptosis, comprising detecting SEQ ID NO:7 in the cytoplasm of said cell.

10 45. The method of Claim 44, wherein said method further comprises quantifying the level of the detected SEQ ID NO:7.

15 46. A method for detecting disease in a mammalian animal, comprising detecting SEQ ID NO:7 in the blood of said mammalian animal.

47. The method of Claim 46, wherein said disease is associated with cell death.